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Radiofrequency ablation (RFA) as a cytoreductive strategy for hepatic metastasis from breast cancer

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ABSTRACT

INTRODUCTION Patients with liver metastasis from breast cancer have a poor prognosis, although this may be improved by hepatectomy in a selected group with disease confined to the liver. We evaluate the effectiveness of radiofrequency ablation (RFA) as a cytoreductive strategy in the management of liver metastasis from primary breast cancer.

PATIENTS AND METHODS Nineteen patients with hepatic metastasis from primary breast cancer underwent RFA of their liver lesions between April 1998 and August 2004.

RESULTS The median age of the patients was 52 years (range, 32–69 years), 8 had disease confined to the liver, with 11 having stable extrahepatic disease in addition. Seven patients with disease confined to the liver at presentation are alive, as are 6 with extrahepatic disease, median follow-up after RFA was 15 months (range, 0–77 months). Survival at 30 months was 41.6%. In addition, 7 patients followed up for a median of 14 months (range, 2–29 months) remain alive and disease-free. RFA failed to control hepatic disease in 3 patients. RFA was not associated with any mortality or major morbidity.

CONCLUSIONS Control of hepatic metastasis from breast cancer is possible using RFA and may lead to a survival benefit, particularly in those patients with disease confined to the liver.

KEYWORDS

Liver metastasis – Radiofrequency ablation (RFA) – Breast cancer

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Patients with metastatic breast cancer have a poor prognosis and are considered to have disseminated disease even if that disease appears to be localised to a single organ. A small group of patients with metastasis confined to the liver (5–12%)[1] appear[2] to have an improved prognosis following hepatic resection and 3-year survival rates of 35–71% have been reported although disease-free survival rates are considerably lower.[3–6] It has been suggested that hepatic resection improves survival by means of reducing the tumour burden of the patient, thus allowing subsequent hormonal or chemotherapy to be more effective.[7,8] Radiofrequency ablation (RFA) is a relatively simple percutaneous technique that has been demonstrated to be an effective cytoreductive strategy for a variety of metastatic liver malignancies, with few side effects and little disruption of the patients life.[9,10] We report our experience using RFA in patients with metastatic liver disease from primary breast cancer.

Patients and Methods

Nineteen patients with hepatic metastasis from primary breast cancer underwent RFA of their liver lesions between April 1998 and August 2004. Patients were referred at the discretion of oncologists from other institutions and relied upon their existing knowledge of the effectiveness of RFA in other forms of cancer; there was no formal selection criteria. Following staging that included an isotope bone scan and CT scan of chest, abdomen and pelvis, patients were considered suitable if they had disease confined to the liver or liver disease with stable extrahepatic disease. RFA was performed percutaneously using either ultrasound and CT or magnetic resonance imaging guidance. General anaesthesia was preferred but RFA was performed using local anaesthetic with sedation if necessary. Single or triple-cluster 17-G internally cooled RFA electrodes (Valleylab, Tyco Healthcare, Boulder, CO, USA) were used with RF

Table 1 **Patients treated with RFA**

Patient	Age at first RFA (years)	No. of liver meta-stases	Size of largest metastasis (cm)	Hepatic disease controlled with ablation	Extra hepatic disease (EHD)	No. of RF treat-ments	Follow-up from ablation	Dead/ alive	Follow-up from diagnosis of liver metastasis	Liver or EHD present
1	62	8	1.5	Yes	Bone	1	0	Alive	2	
2	33	3	2.6	Yes	No	1	2	Alive	14	
3	32	1	3.5	Yes	Cervical lymphadenopathy	1	4	Dead	8	EHD
4	43	1	4.2	Yes	No	1	7	Alive	14	
5	46	4	4	No	No	1	8	Dead	21	Liver
6	67	7	2	No	Lung/bone/ mediastinal lymphadenopathy	1	9	Dead	30	Both
7	43	1	3	Yes	No	2	10	Alive	13	
8	55	1	3.5	Yes	Mediastinal lymphadenopathy	1	12	Dead	18	EHD
9	33	3	3	Yes	No	2	15	Alive	23	
10	52	1	7.3	No	Bone/Skin	3	15	Dead	38	Liver
11	47	1	2	Yes	Lung	1	16	Alive	19	
12	37	1	2	Yes + chemo	No	3	17	Alive	29	
13	53	1	2	Yes + chemo	Para-aortic lymphadenopathy	1	18	Alive	30	
14	67	5	2	Yes	No	1	30	Alive	31	
15	52	1	3	Yes	Bone/pleural	2	34	Dead	36	EHD
16	69	3	2	Yes	Bone	1	38	Dead	46	
17	42	2	1.4	Yes	Bone	3	48	Alive	53	
18	68	1	4.3	Yes	Pleural	3	50	Alive	56	Liver
19	55	1	3	Yes	No	2	77	Alive	80	EHD

energy applied at a maximum power of < 150 W for 5–10 min. Multiple placements were required to treat patients with metastasis > 1 cm in diameter or with multiple tumours. All patients were allowed to commence a full diet following the procedure and remained in hospital overnight. Pain, low-grade fever and malaise were managed with oral diclofenac 50 mg, three times a day. Patients underwent a further CT scan the following morning, prior to discharge. Oral analgesia was prescribed for 5 days and discontinued at the patients own discretion. Follow-up for recurrent hepatic disease was by 3–6 monthly CT scanning of the liver; however, the decision to give further chemotherapy or adjuvant hormonal therapy remained with the referring oncologist.

Results

The median age of patients was 52 years (range, 32–69 years). At presentation, 8 patients had disease confined to

the liver and 11 had stable extrahepatic disease (Table 1). The median follow-up from diagnosis of liver metastasis was 29 months (range, 2–80 months) and 15 months (range, 0–77 months) following RFA. The median number of hepatic metastasis was 1 (range, 1–7) and the mean size 3 cm (SD ± 1.37 cm). Survival at 30 months following diagnosis was 41.6%, although a further 7 patients who had been followed up for a median of 14 months (range, 2–29 moths) remain alive and disease-free.

RFA was successful in controlling liver metastasis in 16 cases. Of those patients with uncontrolled disease, 1 patient had seven liver metastasis, 1 had a single metastasis of 7.3 cm and 1 had four metastasis, the largest being 4 cm in diameter. All of these patients died from hepatic disease, (median survival, 9 months; range, 8–15 months). The patient with four metastases originally had very extensive disease, which responded well to chemotherapy, but recurrent disease occurred post ablation at the sites of disease, which had disappeared with chemotherapy.

Of the remaining patients, 7 required more than one treatment session with RFA, (median, 2; range, 2–3). Of the 8 patients presenting with disease confined to the liver at presentation, 7 remain alive, 6 without evidence of extrahepatic disease, (median follow-up, 12.5 months; range, 2–77 months). The one patient who died had hepatic disease not controlled by RFA. Five of the patients with extrahepatic disease remain alive; 2 of those who died did so from uncontrolled hepatic disease, (median follow-up, 16 months; range, 0–50 months).

Following RFA, all patients tolerated normal diet that evening. Low-grade fever and malaise were common and were directly related to the volume of disease treated. Post procedural pain was minimal and, although subjectively worse in those with lesions at the periphery of liver which may have involved damage to the liver capsule, all symptoms were easily controlled with oral diclofenac. All patients were discharged home following a single overnight in-patient hospital stay without any other complications.

Discussion

The median survival for patients with metastatic breast cancer is 2 years;[7] however, those with hepatic metastasis are thought to carry a worse prognosis. Gregory *et al.*[11] demonstrated that the median survival of patients with secondary liver metastasis from primary breast cancer following chemotherapy was 4.5 months, and even treatment with agents such as docetaxel may only improve survival to 9–14.7 months.[12,13]

Following hepatic resection for metastatic breast cancer, 3-year survival rates of 49–53%[5,6,14] and 5-year survival rates of 18–34% have been reported.[4,14,15] However, recurrent disease is commonly seen in these patients, being detected in all of those followed for > 1 year in one study[5] and 63% of survivors at 3 years in another.[6] Although there appears to be a survival benefit for those undergoing hepatectomy, the numbers included in the studies tend to be small, ranging from 15–54; due to the highly selective nature of the treatment group, a control group is never included. In addition, the natural history of metastatic breast cancer can be highly variable and, although some authors suggest that liver metastases tend to be resistant to hormonal manipulation,[12] analysis of receptor status in those undergoing hepatectomy is conflicting, having been shown either not to influence survival[6] or to reduce the risk of death 3.5-fold when positive.[14] Although the postoperative mortality following hepatectomy has been drastically reduced in recent years, it remains a major undertaking for the patient with a significant associated morbidity (11.5–26%).[5,6,14] In addition, 1.9–73.5% of patients have extensive intra-abdominal disease at the time of surgery leading to abandonment of the procedure and an unnecessary laparotomy.[6,8,14]

The use of RFA as to reduce tumour 'bulk' in conjunction with systemic therapy is attractive and has been shown to be effective in treating 24 patients with 64 liver metastasis from breast cancer, complete necrosis being achieved in 92%.[16] We confirm that RFA is effective at controlling liver metastasis in all but those with either very large metastasis or numerous deposits and suggest that the maximum benefit is gained by those with 5 or fewer deposits or with a maximum diameter of 5 cm. In addition, the 30-month survival in our group (41.6%) is comparable to that reported for patients who underwent hepatectomy and a further 7 patients followed up for less than 30 months remain alive and disease-free.

Although the management of metastatic breast cancer has recently undergone a dramatic change with the wide-spread use of aromatase inhibitors, taxanes, combination chemotherapy and trastuzumab in HER-2 positive cancers which were not commonly available during our study period, our data suggest a possible survival benefit for those with liver metastasis treated by RFA. This benefit may be of particular importance in those with disease confined to the liver; however, similar limitations are present in this study as in the reports of liver resection. These are the small numbers and lack of a control group due to the highly selective nature of the patients. Since RFA is relatively simple to perform, gives rise to few complications, can be carried out with an overnight in-patient stay or day-case and can be safely repeated for recurrent disease, it is an acceptable form of treatment for hepatic metastases. Those who may obtain the maximum benefit from RFA remains unclear and we feel that consideration should be given to including RFA in a randomised trial protocol for patients with breast liver metastases which includes the use of newer chemotherapeutic agents.

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